



A Publication
of Reliable Methods
for the Preparation
of Organic Compounds

Working with Hazardous Chemicals

The procedures in *Organic Syntheses* are intended for use only by persons with proper training in experimental organic chemistry. All hazardous materials should be handled using the standard procedures for work with chemicals described in references such as "Prudent Practices in the Laboratory" (The National Academies Press, Washington, D.C., 2011; the full text can be accessed free of charge at http://www.nap.edu/catalog.php?record_id=12654). All chemical waste should be disposed of in accordance with local regulations. For general guidelines for the management of chemical waste, see Chapter 8 of Prudent Practices.

In some articles in *Organic Syntheses*, chemical-specific hazards are highlighted in red "Caution Notes" within a procedure. It is important to recognize that the absence of a caution note does not imply that no significant hazards are associated with the chemicals involved in that procedure. Prior to performing a reaction, a thorough risk assessment should be carried out that includes a review of the potential hazards associated with each chemical and experimental operation on the scale that is planned for the procedure. Guidelines for carrying out a risk assessment and for analyzing the hazards associated with chemicals can be found in Chapter 4 of Prudent Practices.

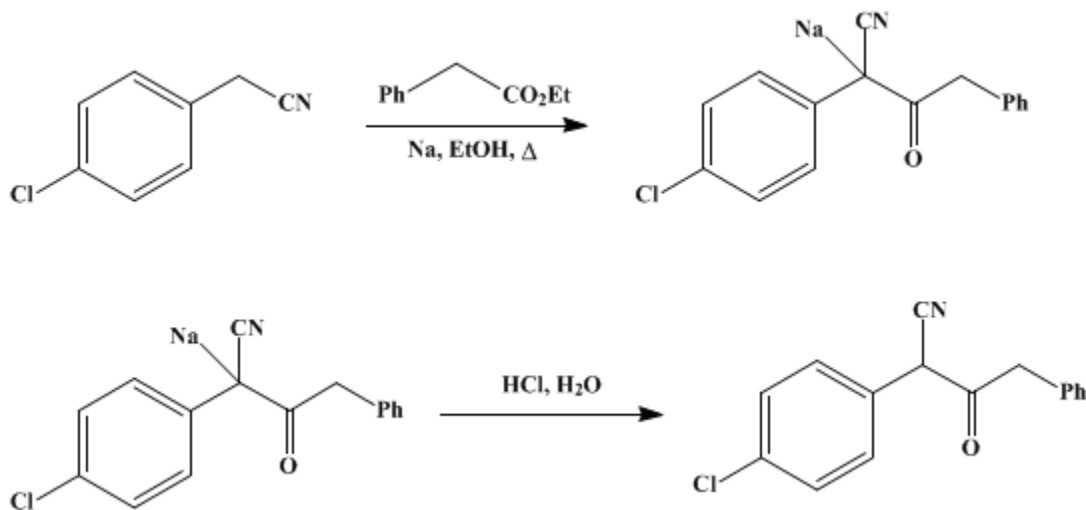
The procedures described in *Organic Syntheses* are provided as published and are conducted at one's own risk. *Organic Syntheses, Inc.*, its Editors, and its Board of Directors do not warrant or guarantee the safety of individuals using these procedures and hereby disclaim any liability for any injuries or damages claimed to have resulted from or related in any way to the procedures herein.

These paragraphs were added in September 2014. The statements above do not supersede any specific hazard caution notes and safety instructions included in the procedure.

Organic Syntheses, Coll. Vol. 4, p.174 (1963); Vol. 35, p.30 (1955).

α -(4-CHLOROPHENYL)- γ -PHENYLACETOACETONITRILE

[Acetoacetonitrile, 2-(*p*-chlorophenyl)-4-phenyl-]



Submitted by Stephen B. Coan and Ernest I. Becker¹.

Checked by Charles C. Price and G. Venkat Rao.

1. Procedure

A solution of 11.5 g. (0.5 g. atom) of sodium is prepared in 150 ml. of absolute ethanol (Note 1) in a 500-ml. three-necked flask equipped with a stirrer, a condenser, and a dropping funnel. While this solution is refluxing with stirring, a mixture of 37.8 g. (0.25 mole) of 4-chlorophenylacetonitrile and 50.8 g. (0.31 mole) of ethyl phenylacetate is added through the dropping funnel over a period of 1 hour. The solution is refluxed for 3 hours, cooled, and poured into 600 ml. of cold water. The aqueous alkaline mixture is extracted three times with 200-ml. portions of ether and the ether extracts discarded. The aqueous solution is acidified with cold 10% hydrochloric acid and extracted three times with 200-ml. portions of ether. The ether solution is then extracted once with 100 ml. of water, twice with 100 ml. each of 10% sodium bicarbonate solution, and once with 100 ml. of water, the aqueous extracts being discarded in turn. The organic phase is dried with anhydrous sodium sulfate, filtered through a fluted filter, and the ether removed by distillation. The yield of α -(4-chlorophenyl)- γ -phenylacetoacetonitrile is 58–62 g. (86–92%), m.p. 128.5–130.0°. For many purposes, this crude product may be used without further purification. If a purer product is desired, however, it may be recrystallized from methanol or aqueous methanol (Note 2) to yield 50–55 g. (74–82%), m.p. 131.0–131.2° (Note 3).

2. Notes

1. Comparable results were obtained when fresh commercial grade (2-B) anhydrous ethanol was used.
2. For recrystallization, a solution of the nitrile in 3–4 ml. of hot methanol per gram was treated with Darco G-60 and filtered on a fluted paper. Distilled water was added to the hot solution until incipient crystallization was observed. In general the final solvent was approximately 90% methanol.
3. The above method has been used in the preparation of other ring-substituted diphenylacetoacetonitriles. The method is equally successful when applied to the condensation of phenylacetonitrile with the ethyl ester of a 4-substituted phenylacetic acid. The table summarizes the results reported by the submitters.

DIPHENYLACETOACETONITRILES

Acetoacetonitrile	Yield, %	M.P.
-------------------	----------	------

From Phenylacetonitrile and an Ethyl 4-Substituted Phenylacetate		
α -Phenyl- γ -phenyl-	82	79.4–80.0°
α -Phenyl- γ -(4-methylphenyl)-	84	88.0–89.0°
α -Phenyl- γ -(4-methoxyphenyl)-	81	69.5–70.4°
α -Phenyl- γ -(4-bromophenyl)-	80	94.0–95.0°
α -Phenyl- γ -(4-methylthiophenyl)-	85	85.0–85.2°
From 4-Substituted Phenylacetonitrile and Ethyl Phenylacetate		
α -(4-Fluorophenyl)- γ -phenyl-	75	111.8–112.0°

3. Discussion

The above procedure is a modification of that described by Walther and Hirschberg.² α,γ -Diphenylacetoacetonitrile has been prepared by the condensation of [phenylacetonitrile](#) with [ethyl phenylacetate](#) in the presence of [sodium ethoxide](#) without solvent.³

This preparation is referenced from:

- [Org. Syn. Coll. Vol. 4, 176](#)

References and Notes

1. Polytechnic Institute of Brooklyn, Brooklyn 2, New York.
 2. Walther and Hirschberg, *J. prakt. Chem.*, [2] **67**, 377 (1903).
 3. Walther and Schickler, *J. prakt. Chem.*, [2] **55**, 305 (1897).
-

Appendix

Chemical Abstracts Nomenclature (Collective Index Number); (Registry Number)

[a-Phenyl-?-phenyl-Acetoacetonitrile](#)

[a-Phenyl-?-\(4-methylphenyl\)-Acetoacetonitrile](#)

[a-Phenyl-?-\(4-methoxyphenyl\)-Acetoacetonitrile](#)

[a-Phenyl-?-\(4-bromophenyl\)-Acetoacetonitrile](#)

[a-Phenyl-?-\(4-methylthiophenyl\)-Acetoacetonitrile](#)

[a-\(4-Fluorophenyl\)-?-phenyl-Acetoacetonitrile](#)

[ethanol \(64-17-5\)](#)

[hydrochloric acid \(7647-01-0\)](#)

[methanol \(67-56-1\)](#)

[ether \(60-29-7\)](#)

sodium bicarbonate (144-55-8)

sodium sulfate (7757-82-6)

sodium (13966-32-0)

sodium ethoxide (141-52-6)

phenylacetonitrile (140-29-4)

Ethyl phenylacetate (101-97-3)

α -(4-CHLOROPHENYL)- γ -PHENYLACETOACETONITRILE,
Acetoacetonitrile, 2-(p-chlorophenyl)-4-phenyl- (35741-47-0)

4-chlorophenylacetonitrile (140-53-4)

Acetoacetonitrile

α,γ -Diphenylacetoacetonitrile